

CLAIMS

1. A method of determining whether an individual has a predisposition to migraine including the step of isolating at least one nucleic acid from said individual that comprises a nucleotide sequence of at least a fragment of a female steroid sex hormone receptor gene, wherein the presence of a polymorphism in said nucleotide sequence indicates that said individual has an increased predisposition to migraine compared to an individual without the polymorphism.
2. The method of Claim 1, wherein said nucleotide sequence is of at least a fragment of exon 8 of a human estrogen receptor (ESR1) gene that encodes codon 594 of an estrogen receptor protein, said individual has an increased predisposition to migraine compared to an individual without the polymorphism.
3. The method of Claim 2, wherein the polymorphism is a guanine to adenine change at nucleotide 2014 of the ESR1 gene.
4. The method of Claim 1, wherein said nucleotide sequence is of at least a fragment of a progesterone receptor gene, wherein said nucleotide sequence comprises a 306 base pair insertion in intron 7 of said progesterone receptor gene.
5. The method of Claim 3, wherein the polymorphism is detected as a restriction fragment length polymorphism.
6. The method of Claim 4, wherein said 306 base pair insertion is detected according to size.
7. The method of Claim 1, wherein two isolated nucleic acids are isolated from said individual, a first nucleic acid comprising a nucleotide sequence of at least a fragment of exon 8 of a human ESR1 gene and a second nucleic acid comprising a nucleotide sequence of at least a fragment of intron 7 of a human progesterone receptor gene.
8. The method of Claim 7, wherein the first nucleic acid comprises a polymorphism that is a guanine to adenine change at nucleotide 2014 of the human ESR1 gene and/or the second nucleic acid comprises a 306 base pair insertion in intron 7 of the human progesterone receptor gene.
9. A method of determining whether an individual has a predisposition to migraine including the step of isolating from said individual

(i) a first nucleic acid that comprises a nucleotide sequence of at least a fragment of a first female steroid sex hormone receptor gene; and

(ii) a second nucleic acid that comprises a nucleotide sequence of at least a fragment of a second female steroid sex hormone receptor gene;

5 wherein the presence of a polymorphism in said first nucleotide sequence of (i) and in said second nucleotide sequence of (ii) indicates that said individual has an increased predisposition to migraine compared to that of an individual having a polymorphism in (i) or (ii) alone.

10 10. The method of Claim 9, wherein said first nucleotide sequence in (i) is of at least a fragment of exon 8 of a human estrogen receptor (ESR1) gene that encodes codon 594 of an estrogen receptor protein.

11. The method of Claim 10, wherein the polymorphism is a guanine to adenine change at nucleotide 2014 of the ESR1 gene.

15 12. The method of Claim 9, wherein said second nucleotide sequence in (ii) is of at least a fragment of a progesterone receptor gene, wherein said nucleotide sequence comprises a 306 base pair insertion in intron 7 of said progesterone receptor gene.

13. The method of any preceding claim, wherein migraine is migraine with aura or migraine without aura.

20 14. A kit for identifying a predisposition to migraine for use in the method of Claim 1, said kit comprising one or more primers for nucleic acid sequence amplification of at least a fragment of a female sex steroid hormone receptor gene.

25 15. The kit of Claim 14, which comprises primers for nucleic acid sequence amplification of at least a fragment of exon 8 of a human ESR1 gene that encodes codon 594 of an estrogen receptor protein.

16. The kit of Claim 15, wherein the kit further comprises a *BtgI* restriction endonuclease.

30 17. The kit of Claim 14, which comprises primers for nucleic acid sequence amplification of at least a fragment of intron 7 of a human progesterone receptor gene.

18. A kit for identifying a predisposition to migraine for use in the method of Claim 9, said kit comprising one or more primers for nucleic acid sequence amplification of:

- (i) a first nucleic acid that comprises a nucleotide sequence of at least
5 a fragment of a first female steroid sex hormone receptor gene; and
- (ii) a second nucleic acid that comprises a nucleotide sequence of at least a fragment of a second female steroid sex hormone receptor gene.

19. The kit of Claim 18, which comprises:

- (a) primers for nucleic acid sequence amplification of at least a
10 fragment of exon 8 of a human ESR1 gene that encodes codon 594 of an estrogen receptor protein; and
- (b) primers for nucleic acid sequence amplification of at least a fragment of intron 7 of a human progesterone receptor gene.

20. The kit of Claim 19, wherein the kit further comprises a *BtgI* restriction
15 endonuclease.

21. A method of determining whether an individual has a predisposition to migraine including the step of isolating a progesterone receptor protein, or fragment thereof, which indicates that said individual has a human progesterone receptor gene polymorphism that indicates an increased predisposition to
20 migraine compared to an individual without the polymorphism.

22. The method of Claim 21, wherein the progesterone receptor protein is detected according to an altered expression level that indicates said individual has a 306 base pair insertion in the human progesterone receptor gene.